To: Ron Kendall, Mark Utell, Cochairs
Samuel Rondberg, Larry Dorsey, DFO's
From: Herbert Needleman M.D.
J Routt Reigart M.D.
June 14, 2000

MINORITY REPORT
DATA FROM THE TESTING OF HUMAN SUBJECTS SUBCOMMITTEE (DTHSS)

We have read the Final Draft of the Subcommittee on Human Testing, and submit this minority report to be made part of the Report. We are compelled to take this step because the Final Draft is a distorted and diluted version of the public proceedings of the Subcommittee. It is a disservice to the efforts of the members, and in the final analysis, to the truth. If accepted, it will serve to increase the health risks of children from pesticide exposure. This is precisely the opposite of the subcommittee's pronounced purpose. As pediatricians whose careers have been dedicated to the prevention of childhood disease, we cannot allow this report to be issued without registering our emphatic dissent.

The authors of the draft, by hindering free access to the record and to communication among members of the subcommittee, permitted this misleading report to be written. At the first subcommittee meeting in December of 1998, strong doubts about both the ethics and scientific validity of exposing humans to organophosphate pesticides were expressed by most of the members. But the first drafts of the proceedings did not reflect this consensus. Although a transcript of the proceedings was promised within 30 days of the meeting, it was not made available until June 1, 1999. As a result, there were no means for members to refresh their memories and test the accuracy of the draft report. Comparing the transcript with the draft reports revealed many misrepresentations of the statements of members.

In June of 1999, four members of the committee signed a minority report (Kendall, Needleman, Reigart, Kahn). That minority report stated that "…the five draft reports of the subcommittee do not accurately reflect the statements made, or the sentiments expressed in that meeting. These members of the Subcommittee expressed many doubts about the acceptability or utility of human testing of pesticides." Four other members, (Caplan, Meslin, Ellis and Gorovitz), signed a letter of support for the minority statement. Including the chairmen, there were 13 members of the Subcommittee.

The final draft differs in no substantial way from earlier flawed versions. It minimizes the risks to humans from intentional experimental dosing, and de-emphasizes the salient issue: that no limited human study will provide information about safe levels of intake of pesticides by humans, especially children. While there was general agreement of the subcommittee that poor science is *per se* unethical, the document gives little credence to the concerns of two highly qualified statisticians (Needleman and Portier). The report gives lip service to the need for large numbers of subjects to achieve adequate statistical power to find a small effect. Calculations of statistical power were submitted at the request of the subcommittee. These provided strong documentation that the human studies done by the pesticide manufacturers were scientifically invalid. They showed that to find a small effect, at least 2500 subjects

in each group were necessary. They also showed that the sample sizes used by the manufacturers, (7 to 50 subjects) to report no effect, had a 3% to 4% chance to find an effect. This was initially placed in the body of the draft, then removed and buried in the appendix, despite the repeated protest of members of the committee.

The Draft paid considerable attention to identifying a rationale for using human adult subjects. It reaches so far as to say that a subject given a pesticide is a potential beneficiary since he or she will encounter the pesticide in the diet. It strains to rationalize the experimental exposure to humans saying: "the overall conclusion appears to be that there are no specific toxicological grounds on which to differentiate pesticides form other environmental chemicals." This is a common assertion of the pesticide industry and its spokesmen. Only one member of the committee advocated this position, but the Draft portrays it as a majority opinion. To make this statement the writer was forced to ignore the provenance of those pesticides that the SAP was asked to examine first: organophosphate pesticides. These compounds originated as military weapons designed to kill people.

The rationale for metabolic studies of pesticides in humans is a pesticidal Trojan Horse: It provides a ready mechanism for dosing humans under the guise of studying metabolic pathways, and then arguing to no effect levels. This intention to use studies with other professed purposes to establish a NOAEL is embodied in this statement in the report "It is agreed that, *generally*, human dosing experiments are not appropriate if the *primary* intent of the study is to determine or revise a NOEL or NOAEL so as to eliminate the interspecies uncertainty factor" (emphasis added). The words "generally" and "primary" provide a loophole that is sufficient to justify any use of research to establish an NOAEL. This clear loophole was inserted in the document despite agreement of the committee that there was no desire to include such inclusions of research which lead to a NOAEL by human dosing.

The inclusion in the "Major Recommendations" of situations under which testing would be appropriate could potentially provide justification for any and all research on humans, as long as IRB approval could be obtained. With the growth of commercial IRB's and extensive opportunities for overseas research such IRB approval is no barrier at all. This recommendation lays the groundwork for a flood of submissions of data from research which should not be conducted and should not be accepted by USEPA for regulatory purposes.

The applicability of adult studies to children's safety is nowhere mentioned in the draft. The Draft acknowledges the enhanced vulnerability of children as a reason to exclude them from dosing. If children are different, then what information can adult dosing provide that is of use to set FQPA standards for protecting children?

These are a few of the many objections that we have to this Report. The others are recorded in our many letters to the DFO. We have worked hard to be heard, and to make the report congruent with the beliefs of the committee as recorded in the two transcripts. The highest goal of pediatric medicine is prevention of illness. This Report does nothing to accomplish this. To the contrary, children will be placed at higher risk of exposure to neurotoxic pesticides if this is allowed to become part of EPA's pesticide policy.